

REMARKS

A Sequence Listing, and a conforming amendment, were filed on August 28, 2002. These presupposed that certain sequences, first disclosed in Serial No. 07/240,160, filed September 2, 1988 (i.e. pre-Sequence Listing rules) did not need to be listed. However, the instant application does not claim the benefit of the '160 application. Hence, a revised sequence listing is required. The substitute sequence listing enclosed herewith is substantially identical to that filed in Ladner=7R, Serial No. 10/207,797.

1. Applicants hereby submit the following:

[XX] a paper copy of a "Sequence Listing", complying with §1.821(c), to be incorporated into the specification as directed above;

[] an amendment to the paper copy of the "Sequence Listing" submitted on , the amendment being in the form of substitute sheets;

[XX] the Sequence Listing in computer readable form, complying with §1.821(e) and §1.824, including, if an amendment to the paper copy is submitted, all previously submitted data with the amendment incorporated therein;

[] a substitute computer readable form to replace one found to be damaged or unreadable.

[] The computer readable form in this application no. 09/... is identical with that filed on [date sequence was filed] in application no. 09/ , filed [filing date]. In accordance with 37 C.F.R. §1.821(e), please use the [first-filed, last-filed or only, whichever is applicable] computer readable form filed in that application as the computer readable form for the instant application. It is understood that the Patent and Trademark Office will make

the necessary change in application number and filing date for the instant application. A paper copy of the Sequence Listing is [included in the originally-filed specification of the instant application, included in a separately filed preliminary amendment for incorporation into the specification, whichever is applicable].

2. The description has been amended to comply with §1.821(d).

3. The undersigned attorney or agent hereby states as follows:

- (a) this submission is not believed to include new matter [§1.821(g)];
- (b) the contents of the paper copy (as amended, if applicable) and the computer readable form of the Sequence Listing, are believed to be the same [§1.821(f) and §1.825(b)];
- (c) if the paper copy has been amended, the amendment is believed to be supported by the specification and is not believed to include new matter [§1.825(a)]; and
- (d) if the computer readable form submitted herewith is a substitute for a form found upon receipt by the PTO to be damaged or unreadable, that the substitute data is believed to be identical to that originally filed [§1.825(d)].

4. Under U.S. rules, each sequence must be classified in <213> as an "Artificial Sequence", a sequence of "Unknown" origin, or a sequence originating in a particular organism, identified by its scientific name.

Neither the rules nor the MPEP clarify the nature of the relationship which must exist between a listed sequence and an organism for that organism to be identified as the origin of

the sequence under <213>.

Hence, counsel may choose to identify a listed sequence as associated with a particular organism even though that sequence does not occur in nature by itself in that organism (it may be, e.g., an epitopic fragment of a naturally occurring protein, or a cDNA of a naturally occurring mRNA, or even a substitution mutant of a naturally occurring sequence). Hence, the identification of an organism in <213> should not be construed as an admission that the sequence *per se* occurs in nature in said organism.

Similarly, designation of a sequence as "artificial" should not be construed as a representation that the sequence has no association with any organism. For example, a primer or probe may be designated as "artificial" even though it is necessarily complementary to some target sequence, which may occur in nature. Or an "artificial" sequence may be a substitution mutant of a natural sequence, or a chimera of two or more natural sequences, or a cDNA (i.e., intron-free sequence) corresponding to an intron-containing gene, or otherwise a fragment of a natural sequence.

The Examiner should be able to judge the relationship of the enumerated sequences to natural sequences by giving full consideration to the specification, the art cited therein, any further art cited in an IDS, and the results of his or her sequence search against a database containing known natural sequences.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

The paragraph on page 155, lines 16-20, has been amended as follows:

```

residue :      17  18  19  20  21  22  23  24  25
5'   g|gcc|gcG|GTA|CCG|ATG|CTG|TCT|TTT|GCT|qfk|qfk|-
      26  27  28  29  30
      |qfk|TTC|TGT|CTC|GAG|cgc|ccg|cga| 3' olig#14 (SEQ ID NO:127)
  
```

The paragraph on page 155, lines 23-27, has been amended as follows:

```

residue :      17  18  19  20  21  22  23  24  25  26
5'   gcc|gcG|GTA|CCG|ATG|CTG|TCT|TTT|GCT|qfk|qfk|qfk|-
      26a 26b  27  28  29  30
      |qfk|qfk|TTC|TGT|CTC|GAG|cgc|ccg|cga| 3' olig#14a (SEQ ID
      NO:128)
  
```

The paragraph on page 155, lines 30-34, has been amended as follows:

```

residue : 17  18  19  20  21  22  23  24  25  26
5'g|gcc|gcG|GTA|CCG|ATG|CTG|TCT|TTT|GCT|qfk|qfk|qfk|-
      26a 26b 26c 26d  27  28  29  30

|qfk|qfk|qfk|qfk|TTC|TGT|CTC|GAG|cgc|ccg|cga| 3'olig#14b (SEQ ID
      NO:129)
  
```

The paragraph on page 216, lines 23-25, has been amended as follows:

```

--M   K   K   S   - rest of VIII
      ACT.TCC.TC.ATG.AAA.AAG.TCT. (SEQ ID NOs:96, DNA,
      and 97)
rest of XI - T   S   S stop--
  
```

The paragraph on page 216, lines 29-31, has been amended as follows:

```
--(L)  K   K   S   - rest of VIII
      ACT.TCC.AG.CTG.AAA.AAG.TCT. (SEQ ID NOS:98, DNA,
      and 99)
rest of XI -T   S   S stop--
```

The paragraph on page 26, lines 11-18, has been amended as follows:

Figure 15 shows the main chain of scorpion toxin (Brookhaven Protein Data Bank entry 1SN3) residues 20 through 42 (SEQ ID NO:274). CYS₃₅ and CYS₄₁ are shown forming a disulfide. In the native protein these groups form disulfides to other cysteines, but no main-chain motion is required to bring the gamma sulphurs into acceptable geometry. Residues, other than GLY, are labeled at the β carbon with the one-letter code.

The paragraph on page 110, lines 7-9, has been amended as follows:

```
      5      6      6      7      7
      5      0      5      0      3
MVVVIVGATIGIKLFKKFTSKAS (SEQ ID NO:122)
```

The paragraph on page 151, lines 33-35, has been amended as follows:

```
      10     11     11     12     12     13
      5      0      5      0      5      0
EYIGYAWAMVVVIVGATIGIKLFKKFTSKAS (SEQ ID NO:273)
```

The paragraph on page 154, lines 13-14 14, has been amended as follows:

```
      84  85  86  87  88  89  90  91
      GGT|GAT|GAT|CCG|GCC|AAA|GCG|GCC|gcg|cc 3' olig#12 (SEQ
ID NO:123)
```

The paragraph on page 154, lines 23-24, has been amended

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as follows:

88 89 90 91
GCC|AAA|GCG|GCC|gcg|cc 3' olig#12a (SEQ
ID NO:124)

The paragraph on page 154, lines 32-33, has been amended
as follows:

88 89 90 91
GCC|AAA|GCG|GCC|gcg|cc 3' olig#12b (SEQ
ID NO:125)

The paragraph on page 154, lines 35-36, has been amended
as follows:

residue 91 90 89 88 87 86
5' gg|cgc|GGC|CGC|TTT|GGC|CGG|ATC 3' olig#13 (SEQ ID NO:126)

The paragraph on page 203, lines 12-13, has been amended
as follows:

Original putative RBS (5'-to-3')

GAGCTCagaggCTTACT**ATGA**AAGAAATCTCTGGTTCTTAAGGCTAGC (SEQ ID NO:130)
|SacI| |Nhe I|

The paragraph on page 203, lines 16-17, has been amended
as follows:

New RBS (5'-to-3')

GAGCTCTggaggaAATAAA**ATGA**AAGAAATCTCTGGTTCTTAAGGCTAGC
|SacI| |Nhe I|
(SEQ ID NO:131)

The paragraph on page 204, lines 2-6, has been amended as
follows:

MB16

5'- GATCC tctagagtcggc TTTACA ctttatgcttc(cg-gctcg...-3'
3'- G agatctcagccg aaatgt gaaatacgaag gc(cgagc...-5'
| | -35 | |
BamHI HpaII
(SEQ ID NOS:132 (top), 133 (bottom))

The paragraph on page 204, line 9, has been amended as follows:

MB22 insert

```
5'- GATCC actcccatcccccctg TTGACA attaatcat -3'
3'-      G tgaggggtagggggac AACTGT taattagtagc-5'
      |         |         |         |
      BamHI      -35|      (HpaII)
(SEQ ID NOS:134 (top), 135 (bottom))
```

The paragraph on page 207, lines 28-30, has been amended as follows:

```
.AAA.GCC.CGT.CCG.GAT.-3' (SEQ ID NO:136)
lys ala arg pro asp..... (SEQ ID NO:137)
      |AccIII|
```

The paragraph on page 208, lines 33-34, has been amended as follows:

```
GCT.CAT.CCG.-3' (SEQ ID NO:138)
ala his pro.... (SEQ ID NO:139)
```

The paragraph on page 222, line 32, has been amended as follows:

```
5'-gttttcagcggCgCCagaatagaaag-3', (SEQ ID NO:140)
```

The paragraph on page 224, lines 1-3, has been amended as follows:

```
5'-TATTCTGGCGCCCGT -3' (SEQ ID NO:141)
3'-ATAAGACCGCGGGCAGGCC-5' (SEQ ID NO:142)
      |NarI| |AccIII|
```

The paragraph on page 317, line 24-page 318, line 9, has been amended as follows:

One mini-protein motif of potential use comprises a disulfide loop enclosing a helix, a turn, and a return strand. Such a structure could be designed or it could be obtained from a protein of known 3D structure. Scorpion neurotoxin,

variant 3, (ALMA83a, ALMA83b) (hereafter ScorpTx) contains a structure diagrammed in Figure 15 (SEQ ID NO:274) that comprises a helix (residues N22 through N33), a turn (residues 33 through 35), and a return strand (residues 36 through 41). ScorpTx contains disulfides that join residues 12-65, 16-41, 25-46, and 29-48. CYS₂₅ and CYS₄₁ are quite close and could be joined by a disulfide without deranging the main chain. Figure 15 shows CYS₂₅ joined to CYS₄₁. In addition, CYS₃₉ has been changed to GLN. It is expected that a disulfide will form between 25 and 41 and that the helix shown will form; we know that the amino-acid sequence shown (SEQ ID NO:274) is highly compatible with this structure. The presence of GLY₃₅, GLY₃₆, and GLY₃₉ give the turn and extended strand sufficient flexibility to accommodate any changes needed around CYS₄₁ to form the disulfide.

The paragraph on page 334, lines 49-52, has been amended as follows:

| | | | | | | | | | | | | | |
|--|-------|--|-------|--|-------|--|-------|--|-------|--|-------|--|------------------------|
| | k | | a | | s | | . | | . | | . | | <u>(SEQ ID NO:123)</u> |
| | 129 | | 130 | | 131 | | 132 | | 133 | | 134 | | |
| | A.A.r | | G.C.n | | T.C.n | | T.A.r | | T.A.r | | T.A.r | | <u>(SEQ ID NO:143)</u> |
| | | | | | A.G.y | | T.G.A | | T.G.A | | T.G.A | | |

At the bottom of page 349, as a new paragraph, please add the following:

Homologues 1-19 are SEQ ID NOs:144-162, respectively.

At the bottom of page 351, as a new paragraph, please add the following:

Homologues 20-35 are SEQ ID NOs:163-178, respectively.

At the bottom of page 353, as a new paragraph, please add the following:

Homologues 36-40 are SEQ ID NOs:179-183, respectively.

At page 362, after the line beginning "ALA58", please add the following as a new paragraph:

(SEQ ID NO:144)

The paragraph on page 366, lines 42-48, has been amended as follows:

| | | | | | | | |
|----------------|---------------|---|---|---|---|---------------------------|-------------------------|
| <u>Sfi</u> I | GGCCNNNNNGGCC | P | 8 | & | 5 | <N,P,T | <u>(SEQ ID NO:184)+</u> |
| <u>Sma</u> I | CCCGGG | P | 3 | & | 3 | <B,M,I,N,P,T | |
| <u>Spe</u> I | ACTAGT | P | 1 | & | 5 | <M,N,T | |
| <u>Sph</u> I | GCATGC | P | 5 | & | 1 | <B,M,I,N,P,T | |
| <u>Stu</u> I | AGGCCT | P | 3 | & | 3 | <M,N,I(<u>Aat</u> I),P,T | |
| % <u>Sty</u> I | CCWWGG | P | 1 | & | 5 | <N,P,T | |
| <u>Xca</u> I | GTATAC | P | 3 | & | 3 | <N(sooN) | |

On page 368, at the end, as a new paragraph, please add the following:

(SEQ ID NO:185)

On page 369, before the last line, please add the following as a new paragraph:

(SEQ ID NO:185)

The paragraphs on page 374, lines 14-21 (ignoring blank lines) have been amended as follows:

| | | |
|---|------------------------|-----|
| s . . . | <u>(SEQ ID NO:187)</u> | |
| 131 132 133 134 | | |
| TCT TAA TAG TGA GGT TAC CAG TCT | | 502 |
| <u>BstE II</u> | | |
| AAG CCC GCC TAA TGA GCG GGC TTT TTT TTT | | 532 |
| <u>Trp terminator</u> | | |
| CCT GAG G -3' <u>(SEQ ID NO:186)</u> | | 539 |
| <u>Sau I</u> | | |

The paragraphs on page 375, lines 14-21 (ignoring blank lines), have been amended as follows:

| s | . | . | . | (residues 128-131 of SEQ ID NO:187)
|131|132|133|134|
|TCT|TAA|TAG|TGA|GGT|TAC|CAG|TCT|
| BstE II |

|AAG|CCC|GCC|TAA|TGA|GCG|GGC|TTT|TTT|TTT|
| Trp terminator |

|CCT|GAG|Gca|ggt|gag|cg - 3' (SEQ ID NO:188)
| Sau I | spacer |

The paragraph on page 376, lines 15-16 (ignoring blank lines), has been amended as follows:

|CCT|GAG|GCA|GGT|GAG|CG (SEQ ID NO:189)
gga ctc cgt cca ctc gc - 5' (SEQ ID NO:190)

The paragraph on page 377, last four lines, has been amended as follows:

| t | s | k | (SEQ ID NO:192)
|127|128|129|
|ACT|TCG|AAa|gcg|gct|gcg| - 3' (SEQ ID NO:191)
| Asu II | spacer |

The paragraph on page 378, lines 14-15 (ignoring blank lines), has been amended as follows:

|ACT|TCG|AAA|GCG|GCT|GCG| (SEQ ID NO:193)
tga agc ttt cgc cga cgc - 5' (SEQ ID NO:194)

The paragraph on page 379, last four lines, has been amended as follows:

| t | s | k | (SEQ ID NO:196)
|127|128|129|
|ttt|acT|TCG|AAa|gcg|tcg|ccg| - 3' (SEQ ID NO:195)
| Asu II |

The paragraph on page 380, lines 13-14, has been amended

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as follows:

|TTT|ACT|TCG|AAA|GCG|TCG|CCG| (SEQ ID NO:197)
aaa tga agc ttt cgc agc ggc -5' (SEQ ID NO:198)

The paragraph on page 381, last 4 lines, has been amended as follows:

| k | l | f | k | k | f | t | s | k | (SEQ ID NO:200)
|121|122|123|124|125|126|127|128|129|
|AAA|CTG|TTT|AAG|AAA|TTT|ACT|TCG|AAa|gcg|tcg|ggc| - 3' (SEQ ID NO:199)
|Asu II| spacer |

The paragraph on page 382, lines 12-13 (not counting blank lines), has been amended as follows:

|AAA|CTG|TTT|AAG|AAA|TTT|ACT|TCG|AAA|GCG|TCT|TGA| (SEQ ID NO:201)
ttt gac aaa ttc ttt aaa tga agc ttt cgc aga act - 5' (SEQ ID NO:202)

The paragraph on page 388, lines 24-29 (not counting blank lines), has been amended as follows:

+
| s | x | e | d | c | m | (SEQ ID NO:203)
| 70 | 71 | 72 | 73 | 74 | 75 |
|TCT|qfk|GAG|GAT|TGC|ATG|C (SEQ ID NO:204) 322
agc *m ctc cta acg tac gca ccc acc -5' (SEQ ID NO:205)
| Sph I| spacer |

The paragraph on page 389, last 5 lines, has been amended as follows:

| g | a | (SEQ ID NO:206)
| 80 | 81 |
|GGC|GCC| (SEQ ID NO:207)
| Bbe I |
| Nar I |

The paragraph on page 390, lines 23-28 (not counting blank lines) has been amended as follows:

+
| s | W | X | d | c | m | (SEQ ID NO:208)
| 70 | 71 | 72 | 73 | 74 | 75 |
| TCG | TGG | qfk | GAT | TGC | ATG | C | (SEQ ID NO:209)
agc acc **m cta acg tac gcg acc tgc -5' (SEQ ID NO:210)
| Sph I | spacer |

The paragraph on page 391, last 5 lines, has been amended as follows:

| g | a | (SEQ ID NO:211)
| 80 | 81 |
| GGC | GCC | (SEQ ID NO:212)
| Bbe I |
| Nar I |

The paragraph on page 392, lines 21-25 (not counting blank lines), has been amended as follows:

| c | r | a | k | (SEQ ID NO:213)
| 61 | 62 | 63 | 64 |
| TGC | CGT | GCT | AAG | C | (SEQ ID NO:214)
acg gca cga ttc gcg acc ggc (SEQ ID NO:215)
| Esp I | spacer |

The paragraph on page 393, last 5 lines, has been amended as follows:

| g | a | (SEQ ID NO:216)
| 80 | 81 |
| GGC | GCC | (SEQ ID NO:217)
| Bbe I |
| Nar I |

On page 397, after line 26, please add as a new paragraph:

(SEQ ID NO:218)

On page 398, after line 26, please add as a new paragraph
(SEQ ID NO:219)

The paragraph on page 401, lines 16-19 has been amended as follows:

| | | |
|-----------------|------------------------|-----|
| S . . . | <u>(SEQ ID NO:220)</u> | |
| 131 132 133 134 | | |
| TCT TAA TGA TAG | <u>GGTTACC-</u> | 486 |
| | <u>BstE II</u> | |

The paragraph on page 401, lines 26-27, has been amended as follows:

aTCGA (GACctgcaggcatgc)-3' (SEQ ID NO:221)
 (SalI) from pGEM polylinker

The paragraph on page 404, lines 16-19, has been amended as follows:

| | | |
|-----------------|------------------------|-----|
| S . . . | <u>(SEQ ID NO:222)</u> | |
| 131 132 133 134 | | |
| TCT TAA TGA TAG | <u>GGTTACC-</u> | 486 |
| | <u>BstE II</u> | |

The paragraph on page 404, lines 26-27, has been amended as follows:

aTCGA GACctgca GGTCGACC ggcacgc-3' (SEQ ID NO:223)
|SalI|

The paragraph on page 410, lines 27-30, has been amended as follows:

| | |
|-----------------|------------------------|
| S . . . | <u>(SEQ ID NO:224)</u> |
| 131 132 133 134 | |
| TCT TAA TGA TAG | <u>GGTTA/CC-</u> |
| | <u>BstE II</u> |

The paragraph on page 410, lines 37-38, has been amended as follows:

a/(TCGA),-3' (SEQ ID NO:225)
 (Sal I)

At the bottom of page 413, please add the following new paragraph:

For oligos #801-808 and 810-817, see SEQ ID NOs:226-241

in Table 105.

The paragraph on page 414, lines 3-11 (not counting blank lines) has been amended as follows:

| Overlap Sequences | Junction | Tm |
|----------------------|----------|---------------------|
| AGGCTTACTATGAAG | 802:817 | 42. (SEQ ID NO:242) |
| TGTCCTTCGCTCG | 803:816 | 42. (SEQ ID NO:243) |
| CTATTTCTACAATGC | 804:815 | 40. (SEQ ID NO:244) |
| AACAACCTTTAAATCG | 805:814 | 38. (SEQ ID NO:245) |
| CCTTCAATTCTCTGC | 806:813 | 44. (SEQ ID NO:246) |
| CGTTGGTGCTACC | 807:812 | 42. (SEQ ID NO:247) |
| CCAGTCTAAGCCC | 808:811 | 42. (SEQ ID NO:248) |

The paragraph on page 415, lines 1 to end, has been amended as follows:

Table 105: Individual sequences of Oligonucleotides 801-817.

Olig #801 (68 bases)

5'-ggcTTTAcAc TTTATgcTTc cggcTcgTAT AATgTgTggA ATTgTgAgcg cTcAcAATTg AgcTcAgg-3' (SEQ ID NO:226)

Olig #802 (67 bases)

5'-AggcTTAcTA TgAAgAAATc TcTggTTcTT AAggcTAgcg TTgcTgTcgc gAcccTggTA cctATgT-3' (SEQ ID NO:227)

Olig #803 (70 bases)

5'-TgTccTTcgc TcgTccggAT TTcTgTcTcg AgccAccATA cAcTgggccc TgcAAAgcgc gcATcATccg-3' (SEQ ID NO:228)

Olig #804 (67 bases)

5'-cTATTTcTAc AATgcTAAAg cAggccTgTg ccAgAccTTT gTATAcggTg gTTgccgTgc TAAgcgT-3' (SEQ ID NO:229)

Olig #805 (76 bases)

5'-AAcAAcTTTA AATcggccgA AgATTgcATg cgTAccTgcg gTggcgccgc TgAAggTgAT gATccggcca Aggcgg-3' (SEQ ID NO:230)

Olig #806 (67 bases)

5'-ccTTcAATTc TcTgcAAgcT TcTgcTAccg AgTATATTgg TTAcgcgTgg gccATggTgg TggTTAT-3' (SEQ ID NO:231)

Olig #807 (69 bases)

5'-cgTTggTgcT AccATcgggA TcAAAcTgTT cAAgAAgTTT AcTTcgAAgg cgTcTTAATg ATAgggTTA-3' (SEQ ID NO:232)

Olig #808 (38 bases)

5'-ccAgTcTAAg cccgccTAAT gAgcgggcTT TTTTTTA-3' (SEQ ID NO:233)

The paragraph on page 416, lines 1 to end, has been amended as follows:

Table 105: Individual sequences of Oligonucleotides 801-817.
(continued)

Olig #810 (29 bases)

5'-TcgATAAAAA AAAAgcccgC TcATTAggc-3' (SEQ ID NO:234)

Olig #811 (69 bases)

5'-gggcTTAgAc TggTAAcccT ATcATTAAgA cgccTTcgAA gTAAAcTTcT
TgAAcAgTTT gATcccgAT-3' (SEQ ID NO:235)

Olig #812 (65 bases)

5'-ggTAGcAccA AcgATAAccA ccAccATggc ccAcgcgTAA ccAATATAcT
cggTAGcAgA AgcTT-3' (SEQ ID NO:236)

Olig #813 (76 bases)

5'-gcAgAgAATT gAaggccgC TTggccggAT cATcAccTTc AgcggcgccA
ccgcAggTAc gcATgcAATc
TTcggc-3' (SEQ ID NO:237)

Olig #814 (67 bases)

5'-cgATTTAAAg TTgTTAcgcT TAGcAcggcA AccAccgTAT AcAAAggTcT
ggcAcAggc TgcTTTA-3' (SEQ ID NO:238)

Olig #815 (72 bases)

5'-gcATTgTAga AATAgcggAT gATgcgcgcT TTgcAgggcc cAgTgTATgg
TggcTcgAgA cAgAAATccg Ga-3' (SEQ ID NO:239)

Olig #816 (65 bases)

5'-cgAgcgAAgg AcAAcATAgg TAccAgggTc gcgAcAgcAA cgcTAGccTT
AAGAAccAgA Gattt-3' (SEQ ID NO:240)

Olig #817 (68 bases)

5'-cTTcATAgTA AgccTccTgA gcTcAATTgT gAgcgcTcAc AATTccAcAc
ATTATAcgAg ccggAAgc-3' (SEQ ID NO:241)

The paragraph on page 417, lines 1 to end, has been amended as follows:

Table 106: Signal Peptides

PhcA M **K** q s t i a l a l l p l l f t p v t **K** A /**R** T... (17)
(SEQ ID NO:249)

MalE M **K** I **K** T G A **R** i l a l s a l t t m m f s a s a l a /**K** I... (18)
(SEQ ID NO:250)

OmpF M M **K** **R** n i l a v i v p a l l v a g t a n a /a **E**... (19)
(SEQ ID NO:251)

Bla M S I Q H F **R** v a l i p f f a a f c l p v f a /h p... (>18)

(SEQ ID NO: 25)

(SEQ ID NO: 254)

(16) (SEQ ID NO:255)

(SEQ ID NO:256)

(16) (SEQ ID NO:257)

(SEO ID NO: 154)

(21) (SEQ ID NO: 258)

(SEQ ID NO:260)

/ Cleavage site

| | | | | | | | | | | | |
|----|----|----|----|----|----|----|----|----|----|----|----|
| 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 |
|----|----|----|----|----|----|----|----|----|----|----|----|

/ cleavage site

| | | | | | | | | | | | |
|----|----|----|----|----|----|----|----|----|----|----|----|
| 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 |
|----|----|----|----|----|----|----|----|----|----|----|----|

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as follows:

```
      G   A   a   e   t   v   e   s   (SEQ ID NO:265)
      77  78  79  80  81  82   83  84
GGc Gcc gct gaa act gtt GAA AGT
```

At the bottom of page 424, please add the following new paragraph:

(SEQ ID NO:266)

The paragraph on page 427, line 16-19, has been amended as follows:

```
| S | . | . | . | (SEQ ID NO:268)
|131|132|133|134|
|TCT|TAA|TGA|TAG|  GGTTACC-
                   BstE II
```

At the bottom of page 427, please add the following new paragraph:

(SEQ ID NO:267)

The paragraph on page 430, lines 24-27, has been amended as follows:

```
| S | . | . | . | (SEQ ID NO:270)
|131|132|133|134|
|TCT|TAA|TGA|TAG|  GGTTACC-
                   BstE II
```

The paragraph on page 430, lines 34-35, has been amended as follows:

```
aTCGA      GACctgca GGTCGAC-3' (SEQ ID NO:269)
                   |SalI|
```

The paragraph on page 433, lines 3-5, has been amended as follows:

```
      1      2      3      4      5      6      7      8      9     10     11     12     13     14     15
fM   K      K      L      L      F      A      I      P      L      V      V      P      F      Y
[G] ATG AAA AAA TTA TTA TTC GCA ATT CCT TTA GTT GTT CCT TTC TAT
|<----- gene III signal peptide ----->
```

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The paragraph on page 437, lines 13-15, has been amended
as follows:

| | | | | | |
|-----|-----|-----|-----|-----|------------------------|
| 481 | 482 | 483 | 484 | 485 | |
| N | K | E | S | . | <u>(SEQ ID NO:272)</u> |
| AAT | AAG | GAG | TCT | TAA | <u>(SEQ ID NO:271)</u> |

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